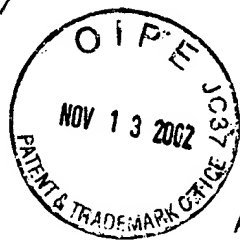


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Attorney Docket No. 18475-025



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT : Lipkowski and Carr
ASSIGNEE : NEW ENGLAND MEDICAL CENTER HOSPITAL
SERIAL NUMBER : 09/988,792 EXAMINER : Vanessa L. Ford
FILING DATE : November 20, 2001 ART UNIT : 1645
FOR : Novel Antimicrobial Agents

November 4, 2002
Boston, Massachusetts

NOV 19 2002

RECEIVED

Commissioner for Patents
Washington, D.C. 20231

DECLARATION OF ANDRZEJ LIPKOWSKI UNDER 37 C.F.R §1.132

I, Andrzej Lipkowski, of Warsaw, Poland, declare and state as follows:

1. I am a co-inventor of the invention claimed in the above-referenced application and am a Professor of Medical Sciences at Medical Research Centre, Polish Academy of Sciences, 5 Pawinskiego St., 02-106 Warsaw, Poland.
2. I hold Ph.D. and D. Sc. degrees from Warsaw University. I have been involved in research relating to neuropeptides and/or antibiotics for the past 33 years.
3. I have reviewed the pending Office Action and the cited prior art, including C. Schroeder, *Acta virol.* 30: 432-435, 1986.
4. I have calculated the molarities of the following antimicrobial concentrations of SP peptides including SEQ ID NO:1, SEQ ID NO: 2, neurotensin and bradykinin, and of Indolicidin, starting with data in the specification of the above referenced application (Table 2 on p. 13) expressed as % solutions.

| | Minimal Inhibitory Concentration MIC (mM) | | | | | |
|-------------|---|----------------|--------------------|--------------------|----------------------|--------------------|
| | <i>S. aureus</i> | <i>E. coli</i> | <i>E. faecalis</i> | <i>P. vulgaris</i> | <i>P. aeruginosa</i> | <i>C. albicans</i> |
| SEQ ID NO:1 | 0.044 | 0.390 | 0.83 | 0.83 | 0.83 | 1.6 |
| SEQ ID NO:2 | 0.76 | 0.76 | 0.76 | 0.76 | 0.76 | 0.18 |
| Neurotensin | 1.3 | 5.2 | 5.2 | 2.6 | 5.2 | >5.2 |
| Bradykinin | 4.0 | 4.0 | >8.0 | 4.0 | 8.0 | 2.0 |
| Indolicidin | 0.014 | 0.032 | n.t* | n.t. | n.t. | 0.070 |

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09/370,793

5. Molarities were calculated using molecular weights (MW) for each compound as follows: substance P (SEQ ID NO:1, triacetate form), the MW is 1528 daltons; for SEQ ID NO:2, the MW is 1695 (triacetate form); for neurotensin, the MW 1672; for bradykinin, the MW is 1240 (triacetate form); for indolicidin, the MW is 2146 (tetraacetate form). Molarity calculations using % solution and the molecular weight of the solute are routine for one of ordinary skill in the chemical arts.

6. The MIC values for bacterial cells were 44 μ M SEQ ID NO:1 and 760 μ M SEQ ID NO:2 for cells of *S. aureus*. The MIC values for fungal cells (*C. albicans*) were 1.6 mM for SEQ ID NO:1 and 200 μ M SEQ ID NO:2. The calculations are correct to the best of my knowledge.

7. The molarities were calculated for the purposes of comparison to data in a reference by C. Schroeder, *Acta virol.* 30: 432-435, 1986. Schroeder describes antiviral activity at 0.6 μ M SP/ Referring to the Table shown in 4 above, the MIC of SP peptides required for anti-bacterial or anti-fungal activity are greater than the concentration described by Schroeder for anti-viral activity. Schroeder does not describe an anti-bacterial nor an anti-fungal activity.

8. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by a fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date Nov. 7, 2002

(Signature)
Andrzej Lipkowski

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